REMARKS

Claims 18-24, 28-35 and 47 are pending in the application. Claim 28 was withdrawn from consideration. In the Office Action dated November 27, 2007, claims 18-24, 29-35 and 47 were rejected. Claims 18-20, 22-24, 29-30, 33-35 and 47 are herein amended to recite that the coating is less than a thickness of the microprotrusions, and claim 21 is accordingly canceled. New claims 51 - 53 are added. Support for the amendments can be found throughout the specification as filed, and at least at paragraphs 0015, 0051, 0061, 0064, 0066 and 0071 of the published application (Appl. Pub. No. 2002/0128599). No new matter has been added. The amendments are being made to expedite prosecution of the application to allowance, and are not to be construed as an admission as to the patentability of the claims as previously filed. In light of the amendments herein, reconsideration and allowance is requested at least for the reasons discussed below.

Applicants note that the Office Action has been designated as Non-Final, despite the statement in paragraph 15 of the Office Action that it is a Final office action. Applicants discussed this discrepancy with the examiner on February 26, 2008, and verified that paragraph 15 was entered in error. Applicants respectfully request acknowledgement from the Examiner that the Office Action is indeed Non-Final.

Claim Rejections under 35 U.S.C. §112

Claims 18-24, 29-35 and 47 have been rejected under 35 U.S.C. §112 1st paragraph as failing to comply with the written description requirement. The Office Action stated that the phrase "... wherein the coating provides systemic delivery of at least 25% of the agent upon application of the device to the skin of a subject for 5 seconds..." is new matter that was not in the original specification as filed.

Without acquiescing to the assertion made in the Office Action, and for the purpose only of expediting prosecution of the application, Applicants have herein amended claims 18-20, 22-24, 29-35 and 47 to strike the above quoted limitation, thus rendering the §112 rejections moot. New claim 51, which depends from claim 19, is herein added to recite that the coating of claim 19 provides systemic delivery of about 25% to 50% of the agent upon application of the

device to the skin of a subject for 5 seconds. New claim 52, which depends from claim 51, is herein added to recite that the pharmacologically active agent comprises desmopressin or hGH. New claim 53, which depends from claim 19, is herein added to recite that the coating of claim 19 provides delivery in the skin of at least about 80% of the agent upon application of the device to the skin of a subject for 5 seconds. Support for these claims can be found at least at paragraphs 0061, 0064, 0066 and 0071, as well as in Figures 8, 9 and 10 of the published patent application (Pub. No. US 2002/0128599).

In response to the statement in the Office Action that there is no indication that other drugs would meet the recited range, Applicants respectfully traverse. The examples described in the specification, at least including Examples 2B, 4B and 6B, demonstrate actual possession of the claimed invention. "Possession may be shown in a variety of ways including description of an actual reduction to practice ..." MPEP §2163 I. (emphasis added). Moreover, in this case, ordinary artisans *could* "predict the operability in the invention of any species other than the one disclosed." MPEP §2163 II. A. 3. (a) (ii). The specification actually demonstrates that the claimed methods are capable of delivering in the skin and systemically a specified amount of a pharmacologically active agent in a specified period of time. The working examples provided in the specification are sufficient to lead one having ordinary skill in the art to apply the invention as claimed to a pharmacologically active agent. Thus the written description requirement for claims 51-53 has been met. Applicants respectfully request reconsideration of the position taken in the Office Action, and allowance of claims 51-53, as well as claims 18-24, 29-35 and 47 as amended.

Claim rejections under 35 U.S.C. §103

As a preliminary matter, Applicants note that claims 18-24, 29-35 and 47 were rejected using the same rationale for each of the following references: U.S. Patent No. 3,470,011 to Szumski et al. ("Szumski"), U.S Patent No. 6,537,242 to Palmer ("Palmer"), U.S Patent No. 6,589,202 to Powell ("Powell"), WO 96/10630 to Trimmer et al. ("the '630 application"), and U.S. Patent No. 5,457,041 to Ginaven et al. ("Ginaven"). Specifically, the Office Action stated that because the agents disclosed by these references are similar to those described in the instant application, the solubility or viscosity of these agents "are expected to be similar." The rejection

made on this ground has not been based on documentary prior art. As the accompanying Declaration by Dr. Yuh-Fun Maa demonstrates, neither general knowledge in the art nor common sense can be used to support the alleged *prima facie* obviousness of the claims. In the absence of documentary prior art or general knowledge in the art, the rationale given in the Office Action amounts to a mere conclusory statement, which cannot be used to support a prima facie finding of obviousness. (See Federal Register 72(195):57526-57535 (Oct 10, 2007)[1]

The Office Action provided no articulated reasoning to support the assertion that the solubility and viscosity of the coatings mentioned in the references are expected to be similar to those recited in the instant claims. In fact, the references themselves suggest the opposite. Note that Szumski – in the context of the disclosed invention – teaches that "over an enormous range," the viscosity of the liquid containing the agent is "immaterial." (Szumski, col. 2, ll. 42-44). Furthermore, Ginaven teaches away from a dipping solution having the range of viscosity recited in the instant claims, suggesting instead that biological substances such as RNA and DNA can be deposited onto a needle array by dipping the array in a carrier suspension comprising a "viscous substance such as glycerol or aqueous poly ethylene glycol, prior to delivery." (Ginaven, col. 4, ll. 29-33). Thus, the viscosity and solubility parameters of the solutions of the claims of the instant application do not form a part of general common knowledge in the art and are not simply a matter of common sense.

In further support of the claims of the instant application, a Declaration by Dr. Yuh-Fun Waa under 37 C.F.R. §1.132 has been submitted herewith. As stated in the Declaration, Dr. Waa is the Director of Formulation and Analytical Development for Zosano Pharma, which is the exclusive licensee of the technology (the Macroflux® dip-coating process) covered by the subject matter of the instant application. He is an expert in the field of pharmaceutical delivery formulations. The Declaration sets forth in detail and establishes the nonobviousness of the claims of the instant application. The viscosity of the solution and solubility of the active agent are shown to be important, and the result of a careful evaluation of the conditions necessary to produce a commercially effective dry agent-containing coating on the member or microprotrusions as claimed herein. Applicants respectfully maintain that in the absence of

[1] Docket No. PTO-P-2007-0031: Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*

documentary prior art teaching the ranges recited in the instant claims, there is no basis to reject the claims on grounds that the solubility and viscosity of the agents disclosed in the references are "expected to be similar" to those of the instant claims. Thus the claims are not obvious under 35 U.S.C. §103(a). Reconsideration of the rejections, and allowance of claims 18-24, 29-35 and 47 is respectfully requested.

Szumski et al.

Claims 18-24, 29-35 and 47 are rejected under 35 U.S.C. §103(a) as being unpatentable over Szumski. The Office Action stated that it would have been obvious to have optimized the size of the tines or the amount of coating to arrive at Applicants' invention. The Office Action also stated that the solubility and viscosity of the agents disclosed in Szumski "are expected to be similar" to those recited in Applicants' claims. Applicants respectfully traverse.

Szumski fails to teach that either solubility or viscosity are important in providing a uniform coating from microprotrusion to microprotrusion, or that the administered agent will be therapeutically effective under the recited conditions. In fact, Szumski teaches that "over an enormous range," the viscosity of the liquid containing the agent is "immaterial." (Szumski, col. 2, ll. 42-44). In contrast, Applicants' claimed invention requires the aqueous solution to have a viscosity at about 25 deg. C of less than about 500 centipoises (claims 18-24, 29, 31-35 and 47) or less than about 50 centipoises (claim 30). The fact that Szumski teaches away from the viscosity requirement of Applicants' claimed invention further substantiates its nonobviousness.

Moreover, Szumski does not disclose, teach or suggest that the coating should be less than a thickness of the microprotrusions, as recited in the claims of the instant application as amended. Thus, Szumski does not render the claims of the instant application obvious. For at least these reasons, Applicants respectfully request reconsideration and withdrawal of the rejections of claims 18-24, 29-35 and 47 under 35 U.S.C.§ 103(a) over Szumski.

Palmer

Claims 18-24, 29-35 and 47 are rejected under 35 U.S.C. §103(a) as being unpatentable over Palmer. The Office Action stated that the needle size disclosed by Palmer overlaps with

that claimed by Applicants. The Office Action also stated that the solubility and viscosity of the agent solutions of Palmer "are expected to be similar" to those claimed by Applicants. Applicants respectfully traverse.

Palmer discloses a skin stretching device to enhance the contact of a skin penetrating member with a skin surface. The penetrating member can be coated with a dried pharmaceutical agent. As discussed above, the Office Action provided no basis for asserting that the solubility and viscosity parameters of the agent solutions of Palmer "are expected to be similar" to those of the instant claims.

Moreover, Palmer does not disclose, teach or suggest that the coating be less that a thickness of the microprotrusions, as recited in the claims of the instant application as amended. Thus, Palmer does not render the claims of the instant application obvious. For at least these reasons, Applicants respectfully request reconsideration and withdrawal of the rejections of claims 18-24, 29-35 and 47 under 35 U.S.C.§ 103(a) over Palmer.

Powell

Claims 18-24, 29-35 and 47 are rejected under 35 U.S.C. §103(a) as being unpatentable over Powell. The Office Action stated that the needle size disclosed by Powell overlaps with that claimed by Applicants. The Office Action also stated that the solubility and viscosity of the agent solutions of Powell "are expected to be similar" to those claimed by Applicants. Applicants respectfully traverse.

Powell discloses an assembly for advancing a skin penetrating device to an operating position for penetrating the skin of a patient. The needles in an embodiment of the device can be coated with a dried or lyophilized pharmaceutical agent, which "is particularly suitable for introducing a vaccine intradermally for efficiently delivering a small amount of the vaccine antigen ..." (Powell, col. 8, ll. 62-65). As discussed above, the Office Action provided no basis for asserting that the solubility and viscosity parameters of the agent solutions of Palmer "are expected to be similar" to those of the instant claims.

Moreover, Powell does not disclose, teach or suggest that the coating be less that a thickness of the microprotrusions, as recited in the claims of the instant application as amended. Thus, Powell does not render the claims of the instant application obvious. For at least these reasons, Applicants respectfully request reconsideration and withdrawal of the rejections of claims 18-24, 29-35 and 47 under 35 U.S.C.§ 103(a) over Powell.

WO 96/10630 (Trimmer et al.)

Claims 18-24, 29-35 and 47 are rejected under 35 U.S.C. §103(a) as being unpatentable over the '630 application. The Office Action stated that it would have been obvious to one of ordinary skill in the art to have optimized the size of the tines or the amount of coating "because they are known to be relevant to transdermal injection." The Office Action also stated that the solubility or viscosity of the agent solution disclosed by the '630 application are expected to be similar to those recited in the instant claims. Applicants respectfully traverse.

The '630 reference teaches microprobes that pierce the membranes of individual cells to deliver biological material into the cytosol of the cells ('630 appl., p. 3). The '630 application also teaches that the liquid biological material is "trapped as meniscus between the microprobes." ('630 appl., p. 11-12). The '630 application does not teach drying the applied aqueous solution to form a dry agent-containing coating on the member having a plurality of stratum corneum-piercing microprotrusions, or on the microprotrusions themselves, as recited in the instant claims.

The '630 application also fails to teach or suggest how to modify a device for the *intracellular* administration of minuscule quantities of an agent (see, e.g., example 2 of the '630 application, in which 2.5 micrograms of a DNA preparation are delivered into a cell) into a device for *transdermally* delivering a pharmacologically active agent, as recited in the instant claims. As discussed above, the Office Action provided no basis for asserting that the solubility and viscosity parameters of the agent solutions of Palmer "are expected to be similar" to those of the instant claims.

Moreover, the '630 application does not disclose, teach or suggest that the coating be less that a thickness of the microprotrusions, as recited in the claims of the instant application as

amended. Thus, the '630 application does not render the claims of the instant application obvious. For at least these reasons, Applicants respectfully request reconsideration and withdrawal of the rejections of claims 18-24, 29-35 and 47 under 35 U.S.C.§ 103(a) over WO 96/10630.

Ginaven et al.

Claims 18-24, 29-35 and 47 are rejected under 35 U.S.C. §103(a) as being unpatentable over Ginaven. The Office Action stated that the animal or plant target cells disclosed in Ginaven would be "inclusive of dermal cells." The Office Action noted that the needles of Ginaven are 25 microns long and 3 microns wide, which overlaps with the sizes claimed by Applicants. The Office Action also stated that the solubility or viscosity of the agent solution disclosed by Ginaven are expected to be similar to those recited in the instant claims. Applicants respectfully traverse.

Ginaven discloses an array of cell piercing micro-needles for intracellular injection of biological substances. (Ginaven, col. 1, ll. 9-18). Ginaven also fails to teach or suggest how to modify a device for the *intracellular* administration of minuscule quantities of an agent into a device for *transdermally* delivering a pharmacologically active agent, as recited in the instant claims. As discussed above, the Office Action provided no basis for asserting that the solubility and viscosity parameters of the agent solutions of Ginaven "are expected to be similar" to those of the instant claims. In fact, Ginaven teaches away from the viscosity ranges recited in the instant claims by suggesting that biological substances such as RNA and DNA can be deposited onto a needle array by dipping the array in a carrier suspension comprising a "viscous substance such as glycerol or aqueous poly ethylene glycol, prior to delivery." (Ginaven, col. 4, ll. 29-33). Therefore, Ginaven does not render the claims of the instant application obvious. For at least these reasons, Applicants respectfully request reconsideration and withdrawal of the rejections of claims 18-24, 29-35 and 47 under 35 U.S.C.§ 103(a) over Ginaven.

Cormier et al.

Claims 18-24, 29-35 and 47 are rejected under 35 U.S.C. §103(a) as being unpatentable over the '292 application. (U.S. Pat. Appl. Pub. No. 2002/0102292). The Office Action stated

that the '292 application teaches coating stratum corneum-piercing microprotrusion arrays with various agents such as peptides, desmopressin, vaccines etc. for transdermal delivery. The Office Action also stated that the solubility or viscosity of the agent solution disclosed by the '292 application are expected to be similar to those recited in the instant claims. Applicants respectfully traverse.

The '292 application is disqualified as prior art under 35 U.S.C. §103(c). The '292 application was filed September 8, 2001, and published on August 1, 2002, well after the date the instant application was filed (i.e., October 26, 2001). At the time the invention of the instant application was made, both the invention and the subject matter of the '292 application were owned by ALZA Corporation or under obligation of assignment to ALZA Corporation. Because the '292 application does not qualify as a reference under 35 U.S.C. §102(a) or (b), it is therefore disqualified as prior art under 35 U.S.C. §103(c)(1). (see MPEP §706.02(l)(1)). A separate Statement of Common Ownership is made on page 18 of this Response, as set forth under the guidelines in MPEP §706.02 (II).

Therefore, the '292 application does not render the claims of the instant application obvious under 35 U.S.C. §103(a). For at least these reasons, Applicants respectfully request reconsideration and withdrawal of the rejections of claims 18-24, 29-35 and 47 under 35 U.S.C. §103(a) over the '292 application.

STATEMENT OF COMMON OWNERSHIP

U.S. Application Serial No. 10/045,842 (U.S. Pub. No. 2002/0128599) and U.S. Application Serial No. 09/950,436 (U.S. Pub. No. 2002/0102292) were, at the time the invention of Application 10/045,842 was made, owned by the ALZA Corporation or under obligation of assignment to ALZA Corporation.

Provisional Double Patenting Rejections

The Office Action has provisionally rejected claims 18-24, 29-35 and 47 on grounds of obviousness-type double patenting, citing Application Nos. 11/034,891, 10/127,108, 10/674,626, 10/972,231, 11/201,625, 11/202,698, and 11/355,856. Applicants gratefully acknowledge that the Examiner has stayed these rejections until subject matter in the instant application is indicated to be allowable.

CONCLUSION

In view of the above amendments and remarks, applicant believes the pending application is in condition for allowance. A petition and fee for a one-month Extension of Time is submitted herewith. Therefore, Applicants believe that this response is timely filed with sufficient fees. If for any reason the fee paid is inadequate or credit is owed for any excess fee paid, the Commissioner is hereby authorized and requested to charge Deposit Account No. **04-1105** referencing Docker No. 80929(303655).

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